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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,945	06/29/2006	Susumu Shiomi	1089.0600000/MAC/DJN	2732

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,945	SHIOMI, SUSUMU	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-18-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Preliminary Amendment filed June 29, 2006 is acknowledged. Claims 1-15 are presented and represent all of the claims under consideration.

A new title and abstract are noted.

An Information Disclosure Statement filed January 18, 2007 is further acknowledged and has been reviewed to the extent each reference is available in the English language and is a proper citation on a U.S. patent.

A list of co-pending and related cases is requested when Applicant responds to this Office Action.

Claims 11-15 provide for the use of menatetrenone, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 11-15 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to the prevention of any cancer, or liver cancer, optionally derived from chronic liver disease or hepatitis virus cirrhosis,

optionally, hepatitis C virus cirrhosis, comprising administering menatetrenone, vitamin K-II, 2-methyl-3-tetraprenyl-1,4-naphthoquinone. The specification does not reasonably provide enablement for the methods of prevention within the full scope of the claimed compound. Further, the specification fails to provide support for the prevention of any cancer derived from chronic liver disease following the administration of menatetrenone.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547, the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is drawn to the prevention of any cancer, or liver cancer, optionally derived from chronic liver disease or hepatitis virus cirrhosis, optionally, hepatitis C virus cirrhosis, comprising administering menatetrenone. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of hepatology.

However, that factor is outweighed by the unpredictable nature of cancer. In cases involving unpredictable factors, such as the instant claims drawn to physiological activity, the scope of enablement varies inversely with the degree of unpredictability of the factors involved. One skilled in the chemical or biological arts cannot always reasonably predict how different chemical compounds might behave under varying circumstances. See *Ex parte Sudilovsky* 21 USPQ2d 1701.

The instant specification (pages 5-8) is drawn to showings of female subjects having virus cirrhosis, in particular, patients infected with hepatitis B or C virus. With respect to cancer development, Figure 1 shows the cumulative incidence of liver cancer patients in the treatment group was smaller than that in the control group. Additionally, Tables 2 and 3 are drawn to odds for developing hepatocellular carcinoma based on blood levels of bilirubin, albumin, platelets, alanine aminotransferase, α-fetoprotein and whether or not interferon had been previously administered. This disclosure does not provide support for preventing any cancer, or liver cancer, optionally derived from chronic liver disease or hepatitis virus cirrhosis, optionally, hepatitis C virus cirrhosis, comprising administering menatetrenone. The instant disclosure is not commensurate in scope with the present claims.

Further, according to The Merck Manual, which is presented for evidentiary purposes only, the prognosis for hepatocellular carcinoma is usually grim. Treatment is generally unsatisfactory. Thus, an assertion of preventing liver cancer is highly unpredictable. The skilled artisan would not reasonably expect vitamin K-II could be safely administered to prevent any cancer, or liver cancer, optionally derived from chronic liver disease or hepatitis virus cirrhosis, optionally, hepatitis C virus cirrhosis.

The amount of direction or guidance provided and the presence or absence of working examples

A working example drawn to a prevention modality is absent. Support for the claimed invention is solely directed to inhibiting the incidence of hepatocellular carcinoma in women presenting with hepatitis B or C virus. No other types of cancer

are supported by any evidence whatsoever. No other chronic liver disease, such as alcoholic liver disease or fibrosis of the liver, is described. No guidance is provided drawn specifically to methods of prevention, as defined by the instant claims. Such an assertion is beyond the scope of the instantly claimed invention. The term "prevention" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases suffered by mankind cannot be totally prevented with current therapies.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to other disease states other than hepatocellular carcinoma. The skilled artisan would expect the administration of menatetrenone in the prevention of cancer to be very specific and highly unpredictable absent a clear understanding of the structural or pathological basis in a preventative modality. The instant specification sets forth no such understanding. No direction is provided to distinguish therapy among various cancers that are encompassed in the claim language. Absent reasonable *a priori* expectations of success for using menatetrenone, one skilled in the hepatology art would have to test extensively various pathologies to discover which in particular exhibits a preventative effect. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Prevention entails the complete and absolute inhibition of the onset of a cancer entirely.

Due to the known unpredictability of the art, and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that any cancer, or liver cancer, optionally derived from chronic liver disease or hepatitis virus cirrhosis, optionally, hepatitis C virus cirrhosis, comprising administering menatetrenone could be prevented. Accordingly, the instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Koike et al., US 2005/0075404.

Koike teaches an agent comprising menatetrenone for inhibiting hepatocellular carcinoma. See page 1, paragraph [0008], and page 2, paragraph [0037].

Intended use confers no patentable weight to composition claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koike et al., US 2005/0075404, in view of The Merck Manual.

Koike teaches an agent comprising menatetrenone for inhibiting hepatocellular carcinoma. See page 1, paragraph [0008], and page 2, paragraph [0037]. The Merck Manual teaches chronic hepatitis B infection is largely responsible for the high prevalence of hepatocellular carcinoma.

Therefore, in view of the combined teachings of Koike and The Merck Manual, one skilled in the art would have been motivated to administer menatetrenone to inhibit the growth of hepatocellular carcinoma. Koike teaches the efficacy of vitamin K-II, while Merck establishes the association between chronic liver disease and the occurrence of frank carcinoma.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 591-272-

0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phyllis G. Spivack/
Phyllis G. Spivack
Primary Examiner
Art Unit 1614

February 29, 2008